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REMARKS

Claims 25-30, 50 and 57 are pending. Claim 25 is amended as described below. It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Rejection of Claims 25 and 26-30, 50 and 57 under 35 U.S.C. 112 (New Matter)

Claims 25 and 26-30, 50 and 57 are rejected under 35 U.S.C. 112 as allegedly containing new mater for use of the phrase "non-naturally occurring."

Applicants respectfully submit that the specification, although not providing word for word support, clearly discloses "non-naturally occurring" amino acid sequences. Nevertheless, to expedite prosecution, the term has been removed from the claims.

It is, however, respectfully pointed out that the claims recite the term "variants." Although the Examiner previously took the position that "variants" can be "wild-type sequences", this position is contrary to the way the term is used and defined in the specification, In particular, the term variant is used in the specification to refer to a non-naturally occurring amino acid sequence in which humans have intervened by altering the amino acid sequence. See the specification at page 3, lines 12 to page 4, line 20, page 15, line 18 to page 16, line 37, in particular, page 16, lines 15 and 16 (defining a "substitution" in relation to *replacing* one amino acid with a different amino acid). Thus, although the Examiner is using the term "variant" to encompass wild-type sequences, this is not how the term is used in the specification or claims, and is not how it would be understood by the skilled artisan.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

II. The Rejection of Claims 25-30, 50 and 57 under 35 U.S.C. 112 (Enablement)

Claims 25-30, 50 and 57 are rejected under 35 U.S.C. 112 as lacking enablement. This rejection repeats essentially the same arguments presented by the Examiner in the prior Office actions. This rejection is respectfully traversed.

35 U.S.C. 112, first paragraph, mandates that the specification teach a person skilled in the art how to make and use the full scope of the invention without "undue experimentation." Determining whether there is undue experimentation requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. See In

re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988). The Federal Circuit in *In re Wands* set forth a number of factors which courts might consider in determining whether a disclosure requires undue experimentation, including (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill in the art, (7) the predictability of the art and (7) the breadth of the claims. *Id.*

Foremost, the Examiner has not given proper consideration to many facts which lead to a contrary conclusion that the claims are enabled. Most importantly, the Examiner has not given due consideration to the very high level of skill in the art in relation to the breadth of the claims. As of the time of the invention, it was routine in the art to produce variant enzymes which were at least 90% homologous to a reference sequence. The literature (both scientific and patent) is voluminous in regard to the ability of the artisan to carryout routine processes to produce variant sequences. These skills encompass well known molecular biological techniques for creating diversity form a known sequence, and include, e.g., enzyme isolation techniques and recombinant mutagenesis techniques which are very well know in the art. See, e.g., any of the references relied upon in the prior art rejections discussed below.

The claims recite a degree of homology of at least 90% to SEQ ID NO:12. Based on the high degree of homology recited in the claims, the polypeptides falling within the scope of the claims will have a very high degree of structural and functional similarity to the reference sequence. As such, an artisan would have a reasonable expectation of being able to practice the claimed invention commensurate in scope with the claims as an artisan is routinely able to obtain, using, e.g., the reference sequence as a starting point, highly homologous sequences therefrom. Indeed, once apprised of Applicants' invention, it is simply routine to practice the invention using well-known molecular biological techniques used for obtaining highly homologous polypeptides.

The test for determining enablement is not whether *any* experimentation is required, but rather whether *undue* experimentation is required. Indeed, and as noted by the *In re Wands* court (*In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), the test for determining whether undue experimentation is required even permits a considerable amount of testing. The experimentation that would be required by the present invention is clearly not undue, but rather involves only routine molecular biological techniques. In this regard, the Examiner has stated that, at a minimum, the number of variants to screen is 19^{485}, and indicates that without guidance for selection of which variant has the desired activity the artisan "would be reduced to the necessity of producing and testing all of the at least 19^{485} possible variants." This statement is clearly incorrect

and also misses the point of a proper enablement analysis. Foremost, no where do the claims require the artisan to make all possible variants. Rather, the claims recite a scope which an artisan can reasonably expect the claimed substitutions to apply across. It is reasonable, given the very high level of skill in the art, that an artisan would be able to make the claimed variant in highly homologous sequences (e.g., at least 90% homology to SEQ ID NO:12). The artisan can make as many variants as they would like or as few as they would like.

In this regard, the Examiner's rejection goes to the specific warning the Federal Circuit set forth in *Hybritech v. Monoclonal Antibodies*, Inc., 231 USPQ 81 (Fed. Cir. 1986) that it is the *nature* and not the *amount* of experimentation that is determinative of non-enablement. The guidance is even more applicable to the present rejection because the Examiner is not simply relying on the amount of *actual* testing required, but by an amount of testing that is not required by claims and instead could *possibly* be performed. That is, an artisan can apply the invention to make one single variant that is 90% homologous to the reference sequence and is not required to screen 19^{485} variants.

The Examiner alleges that the art does not typically engage in the screening of 19^{485} variant. However, this argument again misses the point as the art *does* typically engage in screening vast numbers of variants using routine molecular biological techniques and the artisan is not required by any element of the claim to actually screen 19^{485} variants. Such screening processes are the epitome of routine skills in this art, and the claims simply define the scope at which the artisan can reasonably expect the invention to apply across.

The claims are clearly enabled and the Examiner has not set forth any reason which negates that an artisan can practice the claimed invention commensurate in scope with the claims. Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

III. The Rejection of Claims 25-30, 50 and 57 under 35 U.S.C. 112 (Written Description)

Claims 25-30, 50 and 57 are rejected under 35 U.S.C. 112 as lacking adequate written description support. The Examiners concludes that specification does not provide written description support for the entire genus of claimed "non-naturally occurring" variants. This rejection is respectfully traversed.

The written description requirement of the Patent Code is fulfilled when the patent specification describes the claimed invention in sufficient detail such that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See* Vas-

Cath, Inc. v. Mahurkar, 19 USPQ2d 1111, 1116 (Fed. Cir. 1991). The written description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. *See* In re Marzocchi, 169 USPQ 367 (CCPA 1971).

Under this standard, the Examiner's conclusion that the specification does not provide adequate written description for the claimed invention is incorrect. The specification discloses, and one skilled in the art would clearly recognize, that the scope of the present invention includes variant polypeptides having at least 90% homology to SEQ ID NO:12. Examples of variants falling within the scope of the claimed invention include variants having conservative amino acid substitutions in the amino acid sequence of SEQ ID NO:12, which are clearly envisioned by an artisan once apprised of Applicants' invention as well as the vast number of variants known in the art as applicable to alpha-amylases within this family. See Applicant's prior response. Accordingly, an artisan would reasonably conclude that Applicants were not only in possession of the variants having the alteration in the amino acid sequence of SEQ ID NO:12, but also that Applicants had possession of highly related sequences, as recited by the claims. Indeed, based on the high level of skill in the art, the phrase "an amino acid sequence having at least 90% homology to SEQ ID NO:12" itself conveys to the artisan that Applicants were in possession of the claimed invention.

Notwithstanding the above, the Examiner has not provided sufficient evidence or reasoning to rebut that the specification provides an adequate written description for highly homologous variants claimed. In this regard, the Examiner contends that a number of additional representative species are required to be disclosed. However, given the high degree of homology recited in the claims, an extremely high degree of predictability exists as to the structure and function of variants falling within the claims.

Therefore, Applicants respectfully submit that the specification contains a sufficient description of the structural and functional characteristics of the claimed polypeptides to fulfill the requirements of 35 U.S.C. 112. Reconsideration and withdrawal of the rejection are therefore respectfully requested.

IV. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 102(b) Outtrup et al. (US 5,824,531 and US 5,856,164)

Claims 25, 27-28 and 30 are rejected under 35 U.S.C. 102(b) as anticipated by Outtrup et al. This rejection is respectfully traversed.

The rejection is improper on its face. The Examiner has not pointed to any passage of these references which teaches a protein having a substitution of a K at an amino acid position selected from the group consisting of 118, 320 and 458. Outtrup et al. does not teach variant enzymes. Outtrup et al. teach the isolation and characterization of wild-type enzymes. The Examiner has not pointed out where in this disclosure that the reference teaches a substitution of a K at an amino acid position selected from the group consisting of 118, 320 and 458. This rejection therefore fails to set forth a proper anticipation rejection as the prior art is missing a critical element of the claimed invention.

The Examiner states that the Office does not have the facilities to compare applicants parent protein to the prior art, however, this statement is not relevant as the prior art clearly fails to teach a variant of the parent protein having a substitution of a K at an amino acid position selected from the group consisting of 118, 320 and 458.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

V. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 102(e)

Claims 25, 27-28 and 30 are rejected under 35 U.S.C. 102(e) as anticipated by any one of 12 listed patents: US Patent Nos: 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,287,826, 6,297,038, 6,361,989, 6,486,113, 6,528,298, 6,673,589, 6,867,031, and 6,887,986. This rejection is respectfully traversed.

The anticipation rejection is improper on its face. The Examiner has not pointed to any passage in any of these 12 patents which teaches a protein having a substitution of a K at an amino acid position selected from the group consisting of 118, 320 and 458. The Examiner simply concludes this without directing applicant to any specific teaching. The Examiner states that the Office does not have the facilities to compare applicants parent protein to the prior art, however, this statement is not relevant as the Examiner has not first established where the prior art teaches a variant of the parent protein having a substitution of a K at an amino acid position selected from the group consisting of 118, 320 and 458.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

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VI. The Rejection of Claims 25, 27-28 and 30 under 35 U.S.C. 103 (Obviousness Type Double Patenting)

Claims 25, 27-28 and 30 are rejected for obviousness type double patenting over US Patents Nos. 6,093,562, 6,187,576, 6,197,565, 6,204,232, 6,297,038 and 6,673,589. This rejection is respectfully traversed.

This rejection is improper on its face. The Examiner has not directed applicant to any passage or claim in these patents which establishes obviousness-type double patenting. In particular, the Examiner has not cited any claim(s) from these patents which the Examiner believes creates an unjustified extension of the right to exclude because they claim obvious variations of the same invention claimed in the instant application. See M.P.E.P. 1504.06. In other words, there is no obviousness type double patenting as the Examiner has not provided claimed subject matter that is the basis for this rejection.

For the foregoing reasons, Applicants submit that the claims overcome this rejection. Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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